We use Fourier Traction Force Microscopy to measure the spatiotemporal evolution of shape and traction stresses and construct traction tension kymographs to analyze cell motility as a function of the dynamics of the cells' mechanically active adhesions (traction adhesions). We show that wild-type cells migrate mainly by forming two stationary traction adhesion sites at their front and back halves, over which the cell body moves forward in a step-wise fashion through periodic axial and, to a lesser degree, lateral contractions. We demonstrate that lateral forces are critical in mediating cell motility and essential for migration on highly adhesive substrates where cells implement two alternate motility modes to achieve migration. Our analysis of two mutant strains that lack distinct F-actin crosslinkers (mhcA- and abp120- cells) also supports a key role for lateral contractions in amoeboid cell motility, while the differences in their traction adhesion dynamics suggest the two mutant strains use distinct mechanisms to achieve migration. The considerable differences we find in both the spatiotemporal organization of traction adhesions and contractility, when comparing to the control wild type, provide insight into the role of the extracellular environment and of key cytoskeletal proteins in cell migration. We propose that these are highly conserved mechanisms, which function in a range of amoeboid cells, including leukocytes, as well as other forms of cell motility.

3973-Pos Board B701

Optimal Cooperative Searching using Purely Repulsive Interactions

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Foraging, either solitarily or collectively, is a necessary behavior for survival that is demonstrated by many organisms. Foraging can be collectively optimized by utilizing communication between the organisms. Examples of such communication range from high level strategic foraging by animal groups to rudimentary signaling among unicellular organisms. Here we systematically study the simplest form of communication via long range repulsive interactions between two diffusing Brownian searchers on a one-dimensional lattice. We show that the mean first passage time for either of them to reach a fixed target depends non-monotonically on the range of the interaction and can be optimized for a repulsive range that is comparable to the average spacing between searchers. Our results suggest that even the most rudimentary form of collective searching does in fact lower the search time for the foragers suggesting robust mechanisms for search optimization in cellular communities.

3974-Pos Board B702

Elastic Moduli of Cells Undergoing Neoplastic Transformation

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Using an Atomic Force Microscope (AFM) with a 5.3 um diameter spherical probe we determined the elastic modulus of human mammary epithelial cells (HMEC) as they undergo neoplastic transformation from normal to immortal, tumorigenic, and finally metastatic. We did the measurements over both cytoplasmic and nuclear regions; and as a function of the cells location with respect to a colony (inside a colony, on the periphery of a colony, isolated cells).Tumorigenic and metastatic cells will grow in multiple layers rather than as a colony when confluence increases. So our measurements do not include the inside of a colony part for tumorigenic and metastatic cells. Normal cells show a significant difference in modulus depending on their colony environment. Measurements to date indicate that the cytoplasmic moduli in these 3 different environments for normal HMEC cells are 220 +/- 40 Pa, 380 +/- 50 Pa, and 650 +/- 70 Pa respectively (modulus +/- sem). We expect to report moduli under similar conditions for immortalized and tumorigenic HMEC cells and metastatic cells known as MDA-MB-231. In addition, for normal HMEC cells, we observe moduli differences due to cellular structures with the nuclear modulus being significantly higher (280 +/- 30 Pa, 680 +/- 90 Pa, and 690 +/- 100 Pa respectively) than the modulus of the cytoplasm. We also plan to report on these structural differences for immortalized, tumorigenic and metastatic versions of HMEC cells.

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3975-Pos Board B703

Mapping Local Nanoscale Changes in Cell Tension and Stiffness by Combinatorial Microscopies

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Cellular processes such as division, migration, and remodeling are clearly dependent in the cytoskeletal network, and its local mechanical properties, including stiffness and tension. We have applied a combinatorial microscopy platform that integrates atomic force microscopy with confocal and TIRF microscopy to examine three different scenarios wherein protein-protein interactions are thought to influence these characteristics. Cell migration is intimately tied to cortical actin organization and cell tension. Understanding how these characteristics are impacted by specific protein-protein interactions will be important for our understanding of metastasis in cancer. Cell integrity and stiffness may also be altered during infection with the parvovirus minute virus of mice, which has been shown to alter the local vimentin intermediate filament network. During cell division, changes in the cytoskeletal network are clearly evident. Quantitatively measuring these changes, in real-time, during the process of cell division will provide unique insights into local changes in membrane stiffness and tension that can be linked to specific developmental pathways.

3976-Pos Board B704

Mechanical Gating Properties of Mscl in Mammalian Cells

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Mechanosensitive channel of large conductance (MscL) is a nonselective channel found in the plasma membrane of *E. coli*. It serves as an emergency release valve that protects cells from lysis by allowing the efflux of osmolytes under acute osmotic downshock. Studies of the MscL in yeast models and reconstituted liposomes have suggested that the channel can directly sense biophysical changes in its membrane environment. In particular, the channel is found to be gated by membrane tension on the order of 7-13 dynes$\cdot$cm^{-2} and can have lower activation threshold with increased hydrophobic mismatch between the channel and lipid bilayer. Although MscL is the best characterized mechanosensitive channel, its mechanical gating and potential modes of activation when expressed in mammalian cells have not been fully investigated. To better understand the channel gating properties in mammalian cells, we employed different methods of mechanical stress application to human retinal pigment epithelial (RPE) cells expressing MscL WT and G22S, a mutant MscL with lower activation threshold. RPE cells were made to express MscL WT and G22S via infection of tetracycline regulated adenovirus vectors. We found that MscL WT and G22S were activated to allow influx of a fluorescent dye that increased with increasing osmotic downshock. Acoustic tweezing, a method akin to magnetic tweezing that applies acoustic pressure to displace microbubbles, was used to exert mechanical stress to the cell membrane. Microbubbles were functionalized to attach either to integrins or to transmembrane transferrin receptors. We found that MscL can be activated and the threshold of activation depends on the coupling of force transduction. Our results suggest that MscL retains its mechanical gating in mammalian cells and support the potential for MscL to be utilized as a mechanosensor in mammalian cells.

3977-Pos Board B705

Coherent Cell Rotation in Confluent Monolayer Sheets

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Cell migrations play a vital role in many physiological motility processes including embryogenesis, wound-healing, immune defense and cancer metastasis. Although much effort has been directed towards motility of individual cells, the mechanisms underpinning collective cell migration remain poorly understood. Here a cell mechanics model incorporated persistent force depending on the memory effect on the past orientation of motion is developed to elucidate the coherent rotation motion of monolayer cells in the absence of external signals. This physical model is able to explain how the cell rotation is coordinated in the systems ranging from several cells to multi-cellular assemblies. We show that the competition between the active persistent and random forces is responsible for the robust rotation motion, where the passive coupling forces between cells is also necessary. It is found that the angular motion mode depends on the geometrical shape of the underlying substrate.

3978-Pos Board B706

Characteristics of Mechanically-Conditioned, Substrate-Free Cardiac Cell Sheets

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Heart failure remains a major cause of global morbidity and mortality. Since the benefits of heart transplantation are constrained by donor scarcity, and the ability of the heart to regenerate following infarction is limited, cell-based therapies have emerged as alternative treatments for the repair of damaged heart tissue. One method, myocardial cell sheet tissue engineering, detaches cultured cells from substrates without disrupting intercellular